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In the Supreme Court of the United States

OCTOBER TERM, 1964.

No. 701.

DR. HENRY TURKEL and UBIOTICA CORPORATION,
Petitioners,

vs.

FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT.

PETITION FOR REHEARING.

LEO E. RATTAY,
1320 National City Bank Building,
Cleveland, Ohio 44114,
Counsel for Petitioners.

THE GATES LEGAL PUBLISHING CO., CLEVELAND, OHIO—PHONE: 621-5647

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(b) Excerpts from proceedings of the U. S. House of Representatives, October 4, 1962, Pages 22320-22321, Congressional Record 12

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PETITION FOR REHEARING.

Petitioner presents its petition for a rehearing of this Court's order dated January 25, 1965, denying the Petition for a Writ of Certiorari to the United States Court of Appeals for the Sixth Circuit, and, in support thereof, respectfully shows:

GROUNDS FOR REHEARING.

1. That Petitioners in this cause have attempted to invoke the jurisdiction of the federal courts, only after a complete exhaustion of the administrative remedies available to them, and only after the subsequent entry by the Food and Drug Administration of a final administrative order.

2. Under the facts in this cause, the refusal of the federal courts to take jurisdiction, in effect, states the

proposition of law, that the Food and Drug Administration, in the enforcement and implementation of the 1962 Amendments to the Federal Food, Drug and Cosmetic Act, is empowered to determine whether the investigational use of any drug or medicine may be conducted, in its sole discretion, and without any right whatever to a review of its determination in the matter.

3. The effect of the decision of the Circuit Court of Appeals thus may constitute an addendum to the 1962 Amendments to the Federal Food, Drug and Cosmetic Act, to-wit: That the Food and Drug Administration has the sole and complete right and power to determine the scientific progress to be made in the future, in that the Food and Drug Administration may arbitrarily, and without any review of its judgment, determine what new drugs may be involved in investigational use, which is a prerequisite for a New Drug Application under the Statutes.

4. In the event that the decision of the Circuit Court of Appeals stands, the Food and Drug Administration can continue to subvert, and act completely contrary to the intention, purpose and direction as determined by Congress in the enactment of the 1962 Amendments to the Federal Food, Drug and Cosmetic Act.

SUPPLEMENTAL STATEMENT.

The Petitioners respectfully reiterate that all available administrative remedies have been exhausted with respect to the continued investigational use of the "U" Series Drugs.

It is respectfully reiterated that the Respondent, Food and Drug Administration, has taken an arbitrary and unreasonable position with respect to the physical abnormality to which the "U" Series Drugs are directed; and such position is recited on page 6, Petitioners' Reply Brief herein; and in part is as follows:

> "* * * It is our opinion that it may be impossible to write suitable labels for efficacy for this product; *in view of the cytogenetic basis of Mongolism, we recommend that you abandon work on this application.*" (Emphasis added.)

This position of the Food and Drug Administration has been rendered absolute and irreversible as a result of the Court's refusal to take jurisdiction over this matter. Thus the medical opinion and judgment of a few doctors of medicine employed by the Food and Drug Administration is absolute and final and upheld; in contradistinction to the medical judgment and investigational results of more than fifty doctors of medicine, who, by and large, are experts in this particular field of medicine.

The facts are that the Food and Drug Administration is thus given the right to state to the estimated five million persons now living in the United States and an estimated 126,000 persons born each year, that they have a condition which because of its "cytogenetic basis," should not be considered in the annals of scientific investigation with the goal in mind to alleviate or treat said physical condition.

There is appended hereto excerpts from the proceedings of Congress, which set forth the intent of Congress as

to the enactment and implementation of the 1962 Amendments to the Federal Food, Drug and Cosmetic Act, 21 U. S. C. 355; and as set forth therein the objective of the 1962 Amendments is:

> "* * * to prevent production under insanitary conditions and to require that the methods used in drug manufacture conform to and are operated and administered in conformity with 'current good manufacturing practice' to the end that the drug 'has the safety and has the identity and strength and meets the quality and purity characteristics which it purports or is reported to possess.'" (Congressional Record—Senate—88th Congress—page 22038.)

Accordingly, it is respectfully reiterated that the opinion and judgment of the Court of Appeals should be reversed and jurisdiction assumed by the Court to review this significant and important cause.

CONCLUSION.

For the foregoing reasons it is respectfully urged that this petition for a rehearing be granted, and that, upon further consideration, writ of certiorari issue to the United States Court of Appeals for the Sixth Circuit.

LEO E. RATTAY,
Counsel for Petitioners.

CERTIFICATE OF COUNSEL.

I, Leo E. Rattay, counsel for the above-named petitioners, do hereby certify that the foregoing petition for rehearing is presented in good faith and not for delay, and that it is restricted to the grounds specified in Rule 58, Subdivision 2, of the Rules of this Court.

LEO E. RATTAY,
Counsel for Petitioners.

EXHIBIT 1.

LEGISLATIVE HISTORY OF 1962 AMENDMENTS OF THE FEDERAL FOOD, DRUG AND COSMETIC ACT, 21 U. S. C. 355.

(a) Excerpts from proceedings of the U. S. Senate, October 3, 1962, Pages 22038, 22039 and 22040, Congressional Record.

SECTION 101—REQUIREMENT OF ADEQUATE CONTROLS IN MANUFACTURING

On this subject the language of the Senate and House bills was identical. The objective is to prevent production under insanitary conditions and to require that the methods used in drug manufacture conform to and are operated and administered in conformity with "current good manufacturing practice" to the end that the drug "has the safety and has the identity and strength and meets the quality and purity characteristics which it purports or is reported to possess."

As the Judiciary Committee had stated:

> The committee decided to provide that not only must the requisite methods, facilities and quality controls be established in conformity with current good manufacturing p actice, but that these methods, facilities and controls must in fact be operated and administered in conformity with current good manufacturing practice.

SECTION 102—EFFECTIVENESS AND SAFETY OF NEW DRUGS

In this important area the language of the Senate and House bills was again identical, with one minor exception. One of the grounds in this section for withholding or withdrawing approval of a new drug application was if, in the

language of the Senate bill, "such labeling is false or misleading in any particular." In the House bill the correlative language was "based on a fair evaluation of all material facts such labeling is false or misleading in any particular." The Senate conferees acceded to the House and the phrase "based on a fair evaluation of all material facts" is contained in the bill reported by the conferees. The grounds of inserting this phrase were stated to be the desire to obviate the possibility that a new drug application would be disapproved or withdrawn arbitrarily or capriciously because of some minor or trivial statement that could be easily corrected but at the same time construed to be false or misleading. This is not a substantive change but an effort to make explicit what would undoubtedly be the case in any event.

Section 103—Records and Reports as to Experience on New Drugs—Approved New Drugs

Both the House and Senate bills added a new provision to the new drug section of the Food and Drug Act requiring drug manufacturers to keep records and make reports as to experience with drugs now on the market. The Senate bill required that in promulgating regulations establishing any recordkeeping and reporting system under this section, the Secretary "shall have due regard for the professional ethics of the medical profession and the interests of patients." In addition the Senate bill authorized the Secretary, where he deemed it appropriate, to furnish drug manufacturers with information on their product that came to the Secretary from sources other than the manufacturer. The House bill contained neither of these provisions. They were accepted by the conferees.

Experimental Use of Drugs

Both the House and Senate bills contain provisions empowering FDA to require drug manufacturers to keep records and make reports on clinical experience with regard to experimental drugs prior to the submission of a new drug application for such product. The keeping of these records and making of reports is made a condition precedent to any experimental program conducted by a drug manufacturer (Italics added). The Senate bill authorized the Secretary to require adequate tests on animals before the drug could be tested on human beings. The House bill contained a similar provision authorizing adequate preclinical tests prior to use of humans. While the House provision was accepted by the conferees, it was specifically provided that "preclinical tests" would include "adequate tests in animals."

The Senate bill also authorized the Secretary to require drug investigators to register with the Secretary. The House bill contained no similar provision and it was not adopted by the conferees. The Senate bill authorized the Secretary to require drug investigators to furnish him with simultaneous copies of their reports to the manufacturer on their experiments with an experimental drug. The House bill, on the other hand, specifically rules out any requirement of direct submission of reports to the Secretary by investigators. The conferees accepted a compromise between the two versions whereby analytical reports made by investigators to the drug manufacturers will be considered as part of the data the Secretary can require drug manufacturers to furnish him prior to the submission of the new drug application in order to enable him to evaluate the safety and effectiveness of the drug in the event a new drug application for it is filed. This new requirement on experimental-use drugs puts a firm legis-

lative and statutory base under FDA existing regulatory power.

With regard to patient consent the Senate bill required that investigators shall have due regard to the "interest of patients," while the House bill specifically required that regulations on experimental-use drugs must condition the use of such drugs on the patient's consent to such use. The conferees adopted substituted language which requires the Secretary of HEW to include in his regulations an experimental drug provision for obtaining patient consent, "except where obtaining such consent would not be feasible, or in the professional judgment of the investigator would be contrary to the best interest of the patient."

The Senator from Nebraska offered the compromise language, and after some rearrangement, it was adopted. It was satisfactory and solved one of the very difficult problems we had in the conference.

The conclusion reached by the conferees with regard to records and reports on new drugs, including experimental drugs, are also applicable to Section 106, Records and Reports as Experience on Antibiotics.

Section 104—New Drug Clearance Procedure

There was only one difference between the Senate and House language with respect to the new drug clearance procedure. Both bills provided that a new drug application cannot become effective automatically under any circumstances but must be affirmatively approved. Both provided that the Secretary initially has 180 days—unless further extended by agreement—in which to decide to approve the application or to give notice of an opportunity for a hearing; that the applicant has 30 days in which to request a hearing; and that the hearing would have to

begin within 90 days after such 30 days, or within a total of 120 days after notice of the opportunity of a hearing. The Senate bill did not set forth any time period by which an order would have to be entered following the hearing. The House bill required the order to be issued in 90 days after the completion of the hearing. A compromise was worked out to the effect that the order would have to be issued within 90 days, not after the hearing, but after the date fixed by the Secretary for filing final briefs. This is the last step in the hearing process prior to the final decision of the Secretary.

I personally felt that the Senate bill, which put no limit on the time that the HEW could take after the hearing, was preferable, but I trust that the present provision will be adequate.

The conferees also accepted a House provision which would correct a needless and unintentional inequity in the application of the food additive anticancer proviso to additives for animal feed, while preserving in its full vigor the consumer protection now afforded by that provision.

The provision stipulates that the anticancer proviso of existing law shall not apply with respect to the use of a substance—for example, a veterinary drug—as an ingredient of feed for animals which are raised for food production, if the Secretary finds, first, that, under the conditions of use and feeding specified in proposed labeling and reasonably certain to be followed in practice, such additive will not adversely affect the animals for which such feed is intended; and, second, that no residue of the additive will be found in any edible portion of such animals after slaughter or in any food product of the living animal—such as milk or eggs.

Another amendment would similarly amend the basic act—which is the corresponding anticancer clause con-

tained in the color additive amendment of 1960 to the basic act.

It should be emphasized that where a new drug is involved in these fields and subsequent information and new evidence raise a question as to its safety, it can be withdrawn under the new withdrawal and suspension powers provided for in Section 102 of the bill.

Section 202—Confidentiality of Information Obtained by Inspection

The House bill extended the scope of the confidentiality requirements in Section 301(j) of the Food, Drug, and Cosmetic Act, but made a special provision to the effect that "nothing in this act shall authorize the withholding of information from the duly authorized committees of the Congress." The conferees decided to strike the confidentiality provsion entirely from the bill and to leave the law on this matter as it is.

The Senate Subcommittee on Antitrust and Monopoly has in the past had no difficulty in securing information from the Food and Drug Administration and has never wished to secure information of the type prohibited by the present law; namely, information relating to "any method or process which as a trade secret is entitled to protection." It is expected, of course, that since the Congress is not making the law more restrictive on this matter, the FDA will not make its interpretation and administration of Section 301(j) more restrictive. Congress and the public deserve to have access to information in the Food and Drug Administration which is not of the nature of a trade secret and is in the public interest.

(b) Excerpts from proceedings of the U. S. House of Representatives, October 4, 1962, Pages 22320-22321, Congressional Record.

STATEMENT

The managers on the part of the House at the conference on the disagreeing votes of the two Houses on the amendments of the House to the bill (S. 1552) to amend and supplement the laws with respect to the manufacture and distribution of drugs, and for other purposes, submit the following statement in explanation of the effect of the action agreed upon by the conferees and recommended in the accompanying conference report:

The House struck out all of the Senate bill after the enacting clause and inserted a substitute amendment.

The committee of conference has agreed in a substitute for both the Senate bill and the House amendment. Except for clarifying, clerical, and conforming changes, the differences are noted below:

EFFECTIVENESS AND SAFETY OF NEW DRUGS

Both the House amendment and the Senate bill required the Secretary of Health, Education, and Welfare to refuse to approve, or to withdraw approval, of a new drug if he found that there was a lack of substantial evidence (as defined) of the effectiveness of the drug for its proposed use, or if he found that the labeling was false or misleading in any particular. The House version required that the finding as to false or misleading labeling be "based on a fair evaluation of all material facts"; the Senate version did not contain the quoted phrase. The conference substitute accepts the House version on this point.

RECORDS AND REPORTS AS TO EXPERIENCE ON NEW DRUGS

Existing law provides that the Secretary of Health, Education, and Welfare shall promulgate regulations for exemption of new drugs from the new drug clearance requirement otherwise applicable under Section 505(1) of the Federal Food Drug, and Cosmetic Act, where such drugs are to be used solely for investigational purposes by qualified experts. The House version provided that regulations of the Secretary could condition such exemption for investigational use of drugs (1) upon submission to him, by the manufacturer or sponsor of the investigation, of reports of the results of preclinical tests conducted before use of the drug on human beings (2) upon the manufacturer or sponsor obtaining signed agreements from each investigator to whom he transmits the drug that patients to whom the drug will be administered will be under the personal supervision of such investigator or of other investigators responsible to him, and (3) upon the establishment and maintenance of records, and the making of reports, of data obtained as the result of such investigational use of such drugs. The House version also provided that the exemption was to be conditioned upon the manufacturer's requiring (1) that experts testing the drug on human beings first inform such patients or their representatives of the experimental nature of the drug and obtain their consent to its use, and (2) that such experts certify that such consent will be obtained.

The committee of conference substituted revised language for the provision of the House version relating to giving information to, and obtaining the consent of, the patients or his representative in connection with the administration of experimental drugs. The conference substitute requires the Secretary to issue regulations con-

ditioning the exemption upon the manufacturer's or sponsor's requiring clinical investigators to certify that where they administer experimental drugs to human beings they will inform them, or their representatives, that the drugs are being used for investigational purposes and obtain their consent, except where providing such information and obtaining such consent would not be feasible, or would, in the professional judgment of the investigator, be contrary to the best interests of those human beings to whom such drugs are being administered. The conference substitute makes clear that the conditions prescribed in the House version are not the sole conditions that may be imposed for the protection of the public health.

Both the Senate and House versions added to the new drug section (Sec. 505) of the Federal Food, Drug, and Cosmetic Act a new subsection (j) authorizing the Secretary by regulation or special order, to require manufacturers of previously cleared new drugs to keep records, and make reports to him, of information obtained by them as to experience with respect to such drugs. The conference substitute provides that the Secretary's regulations or orders under this new subsection, and regulations issued under Section 505(i) with respect to investigational drugs, must have due regard for the professional ethics of the medical profession and the interests of patients, and provides, where the Secretary deems it appropriate, for examination upon request, by persons to whom the regulations are applicable, of similar information received by the Secretary. This provision was in the bill as originally passed by the Senate.